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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,510	09/17/2005	Martin Gimmestad	BAFM0001-100	4461

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EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,510	GIMMESTAD ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,27-29 and 31-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8,9,11,13,14,27-29,31 and 33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/12/08 has been entered.

Claims 1-15, 27-29, 31-37 are pending. Claims 1-15 and 27-36 were examined in the previous action. With supplemental amendment of this application, the applicant, on dates on 2/13/08, cancelled claims 24-26, 30, amended claims 1-4, 14, 27 and added new claims 37. Therefore claims 1-15, 27-29, 31-37 will be examined.

Objections

Objection of Claims 1 & 33, 2&34, 3&35, 4&36, 5&32, 6&29, 11 &31 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn after applicants argument found persuasive.

Claim Rejections

35 U.S.C 112

USC 112 rejection 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 14, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is unclear in recitation of pm promoter and effecter gene XylS as it is unclear what is Pm means and what is the source of XylS gene.

Applicants argument that one knowledgeable in prior art knows what meant by "Pm" and "XylS" is not found persuasive. Applicants need to explain what the terms mean

Claims 2-4 are unclear in recitation of "Biologically pure- -" A biologically pure" bacterial culture of at least one mutant strain--- such a culture can not be biologically pure if it includes more than one strain of a bacteria.

USC 112 rejection 1st paragraph written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6, 8-9, 11, 13-14, 27-29, 31, 33-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of mutant strain

of *P. fluorescens* having alginate production activity wherein one or more alginate biosynthetic pathway genes (such as C-5 epimerase, algG-gene, etc) are mutated by any means . The mutant strain of *P. flurescens* claimed in the instant claims, produced by mutating one or more alginate biosynthetic pathway genes (such as C-5 epimerase, algG-gene, etc) by any means ,is a large variable genus containing many mutant strains from many sources. The specification teaches few mutant strains of *P. fluorescens* (pF201, pf2012,etc recited in claim 5), which do not represent all mutant strains recited in the instant claims. Specification neither teaches the structures of all C-5 epimerase, algG-gene and other alginate biosynthetic pathway genes nor teaches how all *P. fluorescens* strain will be modified. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Applicants argument against 112 written description rejection, described on their amendment pages 8-11, is considered but not found persuasive because although the specification teaches few mutant strains of *P. fluorescens* (pF201, pf2012, these claims encompass the mutant strain of *P. fluorescens* , produced by mutating one or more alginate biosynthetic pathway genes (such as C-5 epimerase, algG-gene, etc) by any means ,is a large variable genus. The genus of *P. fluorescens* strains recited in the claims is a large variable genus that are diverse having a variety of biosynthetic pathway mutant genes. Moreover the genus of *P. fluorescens* strains recited in the claims comprise many mutant strains of *P. fluorescens* having many variants of said alginate biosynthetic pathway genes comprising mutations of the gene itself genes comprising mutating, deleting of any gene fragments encoding specific amino acid residues. Alteration of five genes the specification described does not represents all the variation as described above. As such the strain disclosed are not representative of all the structure and/or function of all strain encompassed by the instant claims. Given this lack of description of representative species encompassed by the genus of the claim, the

specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-4, 6, 8-9, 11, 13-14, 27-29, 31, 33-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the few mutant strain of *P. fluorescens* (pF201, pf2012,etc recited in claim 5) does not reasonably provide enablement for any mutant strain of *P. fluorescens*, produced by mutating one or more alginate biosynthetic pathway genes (such as C-5 epimerase, algG-gene, etc) by any means. The claims broadly recite any mutant strain of *P. fluorescens* produced any means. There are many means of making mutant strain such as mutations of the gene itself, addition of inhibitors, modification of endogenous modulators, mutating, deleting of specific amino acid residues etc., The specification fails to describe how any *P. fluorescens* strain can be mutated by any means to produce alginate in the recited levels.

Claims 1-4, 6, 8-9, 11, 13-14, 27-29, 31, 33-37 are so broad as to include many mutant strains of *P. fluorescens*, produced by mutating one or more alginate biosynthetic pathway genes (such as C-5 epimerase, algG-gene, etc) by any means. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number way of mutating one or more alginate biosynthetic pathway genes to provide mutant strains of *P. fluorescens*,. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a few specific recombinant strains of *P. fluorescens* having specific disclosed mutations of particular genes of the alginate biosynthetic pathway.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Furthermore, there are many means of controlling gene function such as mutations of the gene itself, addition of inhibitors, modification of endogenous modulators, mutating individual nucleic acid, etc. It is not routine in the art to control a gene by any means to obtain desired outcome. Without knowing the structural feature of the protein it encodes, controlling the gene by any means (i.e., such as modification of the gene by mutations) to obtain desired function is unpredictable. Biosynthesis of alginate involves a large number of different enzymes. Controlling one gene without affecting other genes that involve in the alginate synthesis is

difficult. The specification does not support the broad scope of the claims which encompass mutant strains of *P. fluorescens*, produced by mutating one or more alginate biosynthetic pathway genes (such as C-5 epimerase, algG-gene, etc) by any means because the specification does **not** establish: (A) regions of the DNA structure of algG gene which should be modified to control alginate synthesis activity and/or how to control by any means the algG gene or any gene involved in alginate synthesis to obtain desired function without effecting other genes that involve in the alginate synthesis ; (B) the general tolerance of algG gene or other alginate bio-synthetic genes to modification and extent of such tolerance towards controlling the gene with any means; (C) a rational and predictable scheme for modifying any algG residues or residues of other genes with an expectation of obtaining the desired biological function; and / or controlling the gene by any means towards such biological function (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use

the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any mutant strains of *P. fluorescens*, produced by mutating one or more alginate biosynthetic pathway genes by any means. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making mutant strains of *P. fluorescens*, by mutating one or more alginate biosynthetic pathway genes by any means is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants argument against 112 enablement rejection, described on their amendment pages 11-15, is considered but not found persuasive because although specification is **enabled** for a few *P. fluorescens* strains (PF201, Pf2012 and other as recited in claim 5) does not reasonably provide enablement for any *P. fluorescens* strain having mutation of one or more alginate biosynthetic pathway genes by any means as discussed previously.

Applicants argue that the rejection under 35 U.S.C. §112, first paragraph is not proper because applicant's *P.*

fluorescens strains described in the instant claims comprise a genus of *P. fluorescens* strain having mutation of one or more alginate biosynthetic pathway genes. These are not persuasive because these claims encompass *P. flurescens* strain having mutation of any number of alginate biosynthetic pathway genes and mutated by any means. There are many ways to obtain *P. fluorescens* strain *lacking* one ore more alginate biosynthetic pathway genes such as mutations of the entire gene itself, addition of inhibitors, modification of endogenous modulators, modifying other genes involve in the biosynthetic pathway of alginate, etc., many of which require substantially more information than given in specification. Given this lack of description of the means of mutating alginate biosynthetic pathway genes in any *P. fluorescens* encompassed by the genus of the claims, a skilled artisan is not enabled for finding which of enormous number of way as claimed by applicants to mutate any *P. fluorescens* strain. Applicant further argue that *by* random mutagenesis and directed mutagenesis as discussed in the specification one can obtain all those genus of *P. fluorescens* described in the claims. This is not persuasive because *without knowing the structure of the gene encoding*

alginate biosynthetic pathway enzymes *and correlation of the structure of the gene with its function* one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities to find out which amino acid residue to modify, delete or inserted to obtain desired results. This would clearly constitute **undue** experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

CLAIM Rejection - 35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 6, 33-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Huisman et al. (US 2004/0014197) as explained by the previous office action.

Huisman et al. teach mutant strain of *P. fluorescens* (claim 19) producing various polyhydroxy compounds including alginates (claim 5) (upto 80 g/L) wherein *P. fluorescens* strain further is integrated with nuclease gene.

Applicant's argument, that Huisman et al., does not teach *P. fluorescens or* rather any bacterial strain that produce 10g/L alginates is not found to be persuasive because on the contrary Huisman et al teach (see claims 1, 7, 2-3,5) various bacterial strains including *P. fluorescens* wherein 40% dry cell wt is the products

(alginates is one of them) and wherein fermentation process using said strain produce 50g/L cell.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory

period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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